



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/520,470

01/07/2005

Thomas Tuschl

2923-673

5503

6449

7590

11/09/2010

ROTHWELL, FIGG, ERNST & MANBECK, P.C.

1425 K STREET, N.W.

SUITE 800

WASHINGTON, DC 20005

EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

NOTIFICATION DATE

DELIVERY MODE

11/09/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No. 10/520,470	Applicant(s) TUSCHL ET AL.	
	Examiner DANA SHIN	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 45-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8-26-2010</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1635

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on September 13, 2010.

Currently, claims 45-92 are pending and under examination on the merits in the instant case.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

Claims 45-92 remain rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement for the reasons of record as set forth in the Office action mailed on March 11, 2010 and for the reasons stated below.

Applicant's arguments filed on September 13, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims comply with the written description

Art Unit: 1635

requirement because the instant rejection is based on misinterpretation and erroneous reading of the instant specification. In particular, applicant points out that the passages relied on pertain to a method comprising “extracts”, not cells. Since applicant has amended the claims to read only on a mammalian cell, thereby excluding the *Drosophila* embryo lysates disclosed in the specification, applicant's arguments are moot.

Applicant asserts that the claimed subject matter is adequately supported by the specification as evidenced by page 41 that teaches chemical modification for improved nuclease resistance and page 11 that teaches the molecule's length of 14-50 nucleotides. Contrary to applicant's assertions, the specification including pages 11 and 41 does not provide adequate written description for the currently amended claims reading on a single-stranded siRNA-mediated RNAi in a mammalian cell *in vitro*. As noted in the last Office action, the instant specification (see page 36) clearly disclosed that a single-stranded antisense siRNA targeted to lamin A/C reduced lamin A/C expression to "less than 5%" in HeLa (thus mammalian) cells *in vitro* when the siRNA is 5' phosphorylated. Further, as noted in the last Office action, Figure 11 clearly demonstrate that single-stranded siRNAs that are 13-17 nucleotides in length do not inhibit lamin A/C expression in HeLa cells *in vitro* compared to the GL2 siRNA (negative control). Hence, given the evidence of record presented by the inventors themselves, examiner wonders how applicant is able to assert that the claimed subject matter is adequately supported and described by the disclosure of the instant application.

Applicant merely states that “the present inventors have found that single-stranded RNA molecules having at the 5'-terminus at least 15 nucleotides which are completely complementary to a predetermined target transcript have the desired activity.” Contrary to applicant's mere

Art Unit: 1635

statement, a single-stranded siRNA having 15 nucleotides perfectly complementary to a predetermined target transcript (e.g, lamin A/C) is incapable of having RNAi activity or reducing target expression in a mammalian cell *in vitro*. Again, see Figure 11. Further, when the “error bars” are taken into consideration, Figure 11 demonstrates that siRNAs, regardless of the 5' phosphorylation status, which are 17 nucleotides completely complementary to a target transcript are incapable of having the “desired activity”, unless the “desired activity” is no RNAi-inducing activity.

In addition, contrary to applicant's assertion that page 41 that teaches chemical modification for improved nuclease resistance provides adequate support for the claims, the mere disclosure that “chemical strategies” are “available” does not whatsoever indicate that one can perform the claimed “methods” with a chemically modified single-stranded antisense siRNA molecule wherein the molecule contains sugar modifications or backbone modifications at any RNA position or all RNA positions (see for example claim 57 reciting “at least one sugar or backbone modified nucleoside”). That is, there is no adequate description that one can cleave target transcript or activate RISC in a mammalian cell *in vitro* with a single-stranded antisense siRNA that is chemically modified in any and all possible ways as broadly claimed in the instant case. As noted in the last Office action, incorporating chemical modifications at certain positions of the antisense strand of an siRNA molecule was known to abolish RNAi activity. See page 6 of the last Office action. Furthermore, Martinez et al. (*Cell*, 2002) including co-inventors of the present application also taught that chemical modifications at certain positions of the antisense strand inhibits, not activates as claimed in the instant case, RISC activity.

Art Unit: 1635

Since applicant has failed to show that the claimed subject matter is described "in such full, clear, concise, and exact terms" as required by the first paragraph of U.S.C. 112 in spite of the negative data (e.g., Figure 11) presented in the instant application and in view of the state of the art/technology as well as unpredictability pertaining to antisense strand chemical modifications and single-stranded siRNA-mediated target inhibition in "mammalian systems" as recorded in the declaration filed on October 7, 2008, this rejection is maintained.

Double Patenting

Claims 45-92 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17-19, 23-25, and 36-37 of 11/880,355 for the reasons of record as set forth in the Office action mailed on March 11, 2010 and for the reasons stated below.

Applicant's arguments filed on September 13, 2010 have been fully considered but they are not persuasive. Applicant argues that the claims are not obvious because it was hopeless to use a single-stranded RNA molecule for RNAi as indicated on page 8 of the last Office action. Applicant's attention is directed to the fact that the instant double patenting rejection does not rely on the unpredictability factor because it is clear that the invention defined in the instant claims overlaps in scope with the invention defined in the reference claims, wherein the reference claims encompass a single-stranded siRNA-mediated RNAi method "in a cell", which encompasses a mammalian cell as evidenced by the specification of 11/880,355. See page 4: "The present invention also relates to a method of mediating RNA interference of mRNA of a gene in a cell or organism (e.g., mammal such as a mouse or a human)." Hence, the invention

Art Unit: 1635

defined in the instant claims is not patentably distinct from the invention defined in the reference claims. Since applicant's arguments are not persuasive, and since applicant has not filed a signed terminal disclaimer, this rejection is maintained.

New Objections/Rejections Necessitated by Amendment

Claim Objections

Claims 63-66 and 86-89 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 63-66 depend from claim 45 and claims 86-89 depend from claim 69, wherein claims 45 and 69 are currently amended to recite "mammalian cell". Hence, the mere recitation of "eukaryotic cell" or "animal cell" (thus broader in scope than "mammalian cell") or the recitation that "animal cell is selected from the group consisting of a mammalian cell" does not further limit the subject matter of claim 45 and claim 69. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 64 and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1635

Claims 64 and 87 are written to claim a method performed in a "plant cell". However, claims 64 and 87 are inherently limited to a "mammalian cell" by claim dependency. As such, the limitation recited in claims 64 and 87 conflicts with those of previous claims, thereby rendering the claims indefinite.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

Art Unit: 1635

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita (AU1637, Acting SPE) can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Primary Examiner
Art Unit 1635

/Dana Shin/
Primary Examiner, Art Unit 1635